IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



Application of

Joel R. Studin

Serial No.

10/829,315

Filed

April 21, 2004

Examiner

Sheikh, Humera N.

Art Unit

1615

Title

Method and Composition for the Treatment of Scars

Commissioner of Patents and Trademarks P.O. Box 1450 Alexandria, VA 22313-1450

DECLARATION OF JOEL R. STUDIN UNDER 37 C.F.R. §1.132

I do hereby declare as follows:

- 1. THAT I received a Bachelor of Science in General Science and Psychology from the University of Rochester, Rochester, NY, in 1975.
- THAT I received a Doctor of Medicine from Mount Sinai Hospital, New York, NY, in 1982.
- 3. THAT I have practiced as a Plastic and Reconstructive Surgeon since 1987.
- 4. THAT I am the inventor of the above-identified application, that I am familiar with the above-identified application, the Office Actions and applied references rendered to date.
- 5. Exhibit A is a testing report received from Bryce RX Laboratories, Inc., detailing the results of transdermal affect testing conducted by Bryce. I authorized Bryce RX Laboratories Inc. to undertake the transdermal affect testing. All dates and extrancous information have been redacted from Exhibit A.
- Exhibit A reports the transdermal effectiveness evaluation of various possible carriers for delivering topical treatments including corticosteroids for scar tissue, psoriasis, eczema and other cutaneous maladies.

 Transdermal effectiveness was determined by the well-known McKenzie-Stoughton vasoconstriction assay. The McKenzie-Stoughton assay is a skin-blanching test. Under this assay a test sample containing a carrier and hydrocortisone was applied to a test subject's skin and the degree of skin blanching was observed. In accordance with the test, hydrocortisone

adsorbed into the skin causes a localized vasoconstriction at the site of application of the test sample. This vasoconstriction causes the skin to appear white. The more hydrocortisone that was adsorbed into the skin, the whiter the localized spot appeared. At 1, 2, and 4-hour time intervals an observer assessed the amount of skin blanching on a scale of 0 (least blanching) to 4 (most blanching). After all data had been collected from three different observers, the scores were added up to give a total blanching score. The higher the score, the higher the level of blanching, and thus, the higher the level of hydrocortisone adsorbed into the skin.

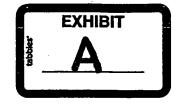
- 7. Exhibit A, page 1, provides further details for the preparation of the samples tested, and testing of those samples. Briefly, 50 ml of a carrier was added to a 200 ml beaker. 1 gm of hydrocortisone was added to the beaker and mixed until fully dissolved. Water was then added to a final volume of 100 ml. According to page 1, a 0.3 cc aliquot of each mixture was placed onto a subjects forearm and marked with a sharpie. Blanching was then observed at 1, 2, and 4-hour time intervals, and vasoconstriction was assessed on a scale of 0 (least blanching) to 4 (most blanching).
- 8. Exhibit A, pages 2-5, provides the blanching results from three observers at 1, 2, and 4-hour time intervals on four different test subjects for each carrier tested. Page 6 provides the cumulative score for each carrier tested for all four test subjects. As can be seen from page 6, Nitrocellulose (Flexible Collodion) had the highest test score (141), which indicates the greatest degree of blanching, and thus, the highest degree of transdermal transmission of the active agent (hydrocortisone) tested.
- 9. Exhibit A, page 6, also provides blanching results for methyl cellulose (14), hydroxymethylcellulose (25), nitrocellulose (flexible collodion/xanthan gum) (59), hydroxyethylcellulose (29), cellulose acetate (23), propylene glycol (7), aluminum hydroxide (49) and tragacanth (3). As can be clearly see from these results nitrocellulose showed very strong transmission of the active agent (hydrocortisone) into the test subject's skin.

10. I further declare that all statements made herein to my knowledge are true and that all statements made on information and belief are believed to be true: and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements so made may jeopardize the validity of the document, or application, or any patent issuing therefrom

Respectfully submitted,

Joel R. Studin

2 21/08



Bryce RX Laboratories, INC. DEA BB5460706

*** TESTING REPORT ***

PAGE i

Formula: Scar/Ecz/Psoriasis

Client: Dr. Joel Studin

TRANSDERMAL AFFECT TESTING SCAR/ECZ/PSORIASIS - DR. STUDIN

The goal of this testing is to ascertain the relative efficacy of a number of possible carriers for delivering topical treatments including corticosteroids for scar tissue, psoriasis, eczema and other cutaneous maladies.

- - METHOD / PROCESS- - - -

Transdermal effectiveness evaluation to be performed using the Coleman, Kanfer and Haigh method of the McKenzie - Stoughton vasoconstriction assay.

- 1. Place 50 ml of carrier into a 200ml beaker
- 2. Place igm hydrocortisone into beaker
- 3. Mix until fully dissolved or evenly dispersed
- 4. Q5 to 100ml
- 5. Seal beaker with plastic wrap
- 6. Repeat for all carriers.
- 7. Place 0.gcc aliquot of each mixture on flexor surface of subject forearm and mark with Sharnie
- 9. Subject to wear short sleeves and avoid washing or sweating
- 9. Observe at 1,2 and 4 hours
- io. Chart observation of skin blanching by subject and z observers
- 11. Vasoconstriction assessed on a scale of zero=least blanching to 4=most blanching

**** THIS TESTING IS A TRADE SECRET OF BRYCE RX LABORATORIES, INC. ****

Methyl Cellulos	e						·.	•	
Observation 1		2,	ahx_	O	4hiz	Q [']	<u>.</u>		•
Observation <u>g</u>	ahr_		zhr_	Q		ହା			
	thr_							Score	2
Hydroxymethylce:	llulose	,							
Observation 1	1hr	1	zhr_	_1	4hr	1			
Übservation <u>a</u>		<u>.</u>	zhr_	1	4hr	_E l			
Subject #1	ihr_	<u> </u>	zhr_	0	4hr	Ø	Total	Score	_5
Nitrocellulose	(Flexible Collod:	ion)							
	1hr		2hr	4	ahr	.1			
Observation 2		А.	2hr	А	abr	4			
Subject #1		3	ahr_	4	4hz	4	_ _Total	Score_	35
Nitrocallulaca	(Flexible Collod:	ian d	Vanada	4 W . C	· 1				
						-			-
Observation a	ihr_			- 6%	# 1.5 e	<u></u>	_		
Subject #1						<u></u>	 T+1	Canna	- .
Dapler: #I		<u> </u>	KIIL		4112	1	_10.49T	score_	14
Hydroxyethylcel:								-	
Übservation 1	1hr		2hr_	1	4hr	æ .	_		
Observation <u>2</u>	1hr	2	ahr_	7.	4hr	G.	_		
Subject #1	1hr_	2	2hr_	ø	4hr	ē.	_Total	Score_	_7
Cellulose Aceta	te								
	ahr_	3.	2hr	7	abr	a			
Observation 2	thr_			<u>-</u>	abr	a			
Subject #s	ıhr_	ନ	anz	0	4\\- ahr	8	— Total	Score	ત્ર
-	-								<u> </u>
Propylene Glyco:	1								
Observation 1	1hr_	1	zhr_	0	4hr	ର			
Observation <u>z</u>	1hr_	1.	zhr_	0	4hr	ø	_		
Subject #1	ahr_	0	2hr_	ō	4hr	್	_Total	Score_	_2
Aluminum Hydros:	ide								
	ıhr_	2	zhr	2	abr	2			
Observation z		2		1	4hr	7	-		
Subject #1		23	shr_	1	4hr	1	_ _Total	Score_	14
Tragacanth									
_	- L	_		_	. 1				
Observation o	1hr 1hr	<u>v</u>		<u> </u>					
Subject #1		ফ						_	
- we led : #1	1hr	0 .	2hr	0	4N£	0	_Total	pcore_	<u> </u>

Methyl Cell							•	•		
Observation	1 1	ihr_	_ 1	ahr_		4hr	ı,		•	
Observation) <u>2</u>	ihr_	- 2	shr_	1.	4hr_	Q.	·		
Subject	#2	դ.hr_	_1	spr	Ď	4hr	ø	_ _Total	Score_	7
	nylcellulose								,	
			_	_ L	_					
	1 1									•
	1 <u>, ż</u>	-				•				_
Subject	#2	16r_	1	2hr_	8	4ħ¥	ତ	_iotal	poore_	<u> </u>
Nitrocellul	ose (Flexible	Collod	ion)							
Observation	1 1	1hr_	_4	ahr_	4	4hr_	ব	_		
	1 2									
Subject	#2	ahr	d	2hr_	đ	4hr_	ä	_ _Tota1	Score_	35
Ni troppi i ul	ose (Flexible	Callad	ion /	Vanah	- C.					
) I						•			
) <u>2</u>								_	
Subject	#2	1nr_		sur-	ପ	4Fix	0	_lotal	pcore_	10
Hydroxyethy	clcellulose									
Observation	1 1	aha	Ē	ahr_	2	4hr	1	_		
	1 2									
Subject	#2	ahr_	1	2hr_	ଡ	4hr	Ø	_Total	Score_	_8_
Cellulose A	inatata	-								
	1 1	a h.s.	7	.abar'		a boss				
	1 <u>2</u>									
	# 注									
Subject	#2			Y X		4rir	<u> </u>	_107aT	phore	4
Propylene 0										
	1									
Observation) <u>s</u>	1hr_	1	zhr_	0	4hr	0	_		
Subject	#2	1hr_	0	zhr	0	4hr	Ø	_Total	Score	2
Aluminum Hy	droxide									
	1	ihr	2	ghr	8	abr	171			
	2							_		
,		ihr_						_ 	Score	10
a sangra o c	n 4-	4114				4' II	ψ	_	7.01 G	
Tragacanth	•		-							
	1		0		ø	4hr_	o	_		
	2	1hr_	ø			4hr_	<u>o</u>	_		
Subject	#2	ahr_	1	zhr_	0	4hr	0	_Total	Score	1

•			•					-	•
Methyl Cel						•		•	. •
Übservatio	า 1		ahr_	1	zhr_		4hr_	Ø	
Observation	ာ <u>ဒ</u> ေ		ıhr_	1	zhr_	_1_	4hr_	0	
Subject	#3		1hr_	ভ	shr_	Ø	4hr_	0	Total Score <u>3</u>
Hydroxymeti	hylce	llulose							•
Observation			ıhr	1	zhr	1	ahr	ı	
Observation	1 2 1						4hr_		
Subject									Total Score7
Nitrocellu:	1050	(Flavihla	· Collada	iani					
Observation					obx		a bos		
Observation	' <u></u>			4.	e,,,_	_4_	411# 4 H.se	<u></u>	
Subject	' <u>=</u>			_4	sur	4	411E	<u> </u>	Total Score <u>96</u>
napliec c	≖⊝		T.I.T	4	201	4	411£	4	
Nitrocellu	lose	(Flexible	Collod	ion, ,	/ Xanth	an G	ium)		
Observation									
Observation	1 <u>2 </u>		1hr_		2hr_	3	4h£_	1	
Subject	#3		ıhr_	3	zhr_	_2_	4hr_	2	Total Score <u>zo</u>
Hydroxyethy	/loe1	lulose							
Observation			1 hr	0	ehr	٦.	abr	à	
Observation									
Subject	#3		hr_	2	zhr_		4hr_	Ð	Total Score <u>a</u>
Cellulose (**							
				_		_			
Observation									
Observation									
phplect	#3		ınr_	<u>ı</u>	2hr_	0	4hr_	0	Total Score <u></u>
Propylene (
Übservation									
Observation	ገ <u>ድ</u>		ihr_	1	shr_	1	4hr_	<u> </u>	<u></u>
Subject	#3		zhr_	1.	anr_	Ø.	4hr_	ମ	Total Score <u>4</u>
Aluminum Hy	/drox	ide							
Observation			ahr_	2	shr_	2	4hr_	ø	
Übservation			ıhr_		zhr_		4hr		-
Subject	#3		1hr		ehr_		4hr		Total Score <u>11</u>
Tragacast							•	• • •	
Tragacanth Observation			- 6		_ [•
Observation Observation			ahr_		zhr_		4hr_		
		· .	1hr_			- 2	4hr_		
Subject	#3		ahr_	0	zhr	ø	4hr	<u> </u>	Total Score <u>ı</u>

Methyl Cell	Lulose		* 1			•			•
Observation	1 1	a.h.x	ତ	ahr_	Q)	_4hr_	0	,	
Observation	1 <u>2 </u>	1hr_	1.	shr	œ	4hr	<u>o</u>		
Subject	#4	1hr_	1	2hr_	क	_4hr_	0	Total	Score <u>z</u>
Hudrosumeth	nylcellulose								
) I	a har		,m, Jro, q.e	_	a linee			
Observation) <u>s</u>	±\\±	- 2			4'''*	_+		
Subject	#4	يا المالي موريط وه		نگالکشر موجود		411£	<u></u>	₩~÷3	· Caasa s
Dan'ies (#4 <u></u>	T11E		WIL	La .	4, II	<u> </u>	idrat	acote
	lose (Flexible C								
Observation	1 1	צולב	4	2nr_	4	_4hr	۵		
Observation	າ <u>ຂ</u>	zhr	4	zhr	4	_45°£	4	,	
Subject	#4	1hr_	3	2hr_	·· <u>4</u>	_4hr_	4	Total	Score <u>at</u>
Nitrocellul	Lose (Flexible C	alladi	ion Z	Xanth.	an Com	1			
	1 1						7		
	2								
	#4								Soore at
			;		A	4''		10.047	70016 <u>78</u>
Hydroxyethy									
Observation	1 1	ahr_	_&	zhr_	0	_4hr_	ø		
Observation	ì <u>2</u>	1hr_	_1	ahr_	<u></u>	_4hr_	Ø		•
Subject	#4	1hr	1	zhr_	0	_4hr_	e e	Total	Score
Cellulose A	netste .								
	1 1	a bar	7	on boson	-	. سويطي			
	1 8								
	#3								Sance O
2000601	Ψ 3			ZIIL	_	_4114		locar	Poore o
Propylene.0	lycol								
Observation	1	_1ht_	Ø	_ahr_	0	_4hr_	ø		
Observation) 2	ihr_	ঠ	ahr_	ଜ	_4hr_	e e		
	#4							Total	Score <u>ø</u>
Aluminum Hv	odrovida								
_	1 1	5 b.s-	~	abr	,	4 box	a		
				ahr				T	-
and Aed r	#4	10 r	2		1	_4nr_	<u> </u>	ıota⊥	500re <u>11</u>
Tragecenth									
Observation	1	_ahr_	8	_žhr	· පු	_4hr_	o		
) <u>S</u>								
	#4	 ihr	٦	_zhr_	8	_4hr		Total	Score 1
-	• •								

BASE CARRIER CUMULATIVE TOTAL SUBJECTS 1-4 [1HR, 2HR, 4HR]

Methyl Cel:	lu1ose		
Subjects	#1-4	Total Score	14
Hydroxymeth	nylcellulose		
Subjects	#1-4	Total Score	<u> 25</u>
Nitrocellul	lose (Flexible	Collodion)	
Subjects	#1-4	Total Score	143
Nitrocellu]	lose (Fléxible	Collodion / Xa	anthan Gum)
Subjects	#1~4	Total Score	<u> </u>
Hydroxyethy	/lcellulose	•	
Subjects	#1-4	Total Score	<u> 24</u>
Cellulose A	loetate		
Subjects	#1-4	Total Score	23
Propylene (Slycol -		
Subjects	#1-4	Total Score	7
Aluminum Hy	/droxide		
Subjects	#1-4	Total Score	49
Tragacanth			
Subjects	#1-4	Total Score	3

Conclusion

Most carriers showed very poor transdermal transmission of the active. Nitrocellulose however, showed a very strong transmission in our formulation. We believe that this is a result of increased bio-electric binding. It is our suggestion that you continue the development of your products using the nitrocellulose base that you suggested.